fallen into the "trap" described in our opening parable. In her chapter on Perspectives, in which she comments on the "Clinical Problems in Cancer Chemotherapy," the author has, in the opinion of this reviewer, seriously detracted from her otherwise informative book. Specifically, she has presented the time-worn argument of "empiricism *vs.* the rational approach" and from a clearly prejudiced viewpoint. Avoidance of this "trap" depends on an awareness that beneficial developments in clinical medicine have most generally resulted from the prudent application of both approaches and that they are not mutually exclusive. Thus, the author criticizes national cancer chemotherapy programs paraphrasing from the 1965 report of the "Wooldridge Committee," which she erroneously states as having been appointed by President Johnson rather than President Kennedy (the final report was made to President Johnson). The author fails to mention that one of the basic recommendations of the Wooldridge Committee was that an *ad hoc* committee be instituted to review the national cancer chemotherapy program. The latter committee, chaired by Arthur P. Richardson, Dean of the Emory University School of Medicine, while recommending some decrease in large-scale empirical anticancer screening and increased emphasis on basic research, did recognize that "... current knowledge of the biology of cancer and mode of action of chemotherapeutic agents is still too limited to support an entirely rational approach."

In the opinion of this reviewer, the national cancer chemotherapy program has, from its inception, recognized the need for both the empirical and rational approach, one complementing the other. One need look no further than the history of modern chemotherapy to become aware that most of man's useful drugs originated with serindipitous or empirical observations followed by developmental work rationally based on structure–activity studies, specificity studies, etc. Discovery by serendipity cannot be planned. It depends on perspicacious observation. Discovery by empiricism is planned and has been successful. It is based on acceptance of the premises that (a) the desired goal exists, and (b) an infinitely broad search will attain the goal or fortuitously uncover a clear way to it which can be followed rationally. If the reviewer seems to make too much of this issue, it is because the author implies that the ability to choose a drug for each patient on the basis of the biological and chemical characteristics of his tumor and the tumor's *in vitro* sensitivity to drugs is a *fait accompli*. The concept is potentially sound, the goal is desirable, but instances of successful application have been rare. In the meantime, while we await the technological developments necessary to achieve this goal, Dr. Knock's immoderate attack on the status of the national program seems premature.

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Progress in Drug Research. Volume 10. Edited by E. JUCKER, Birkhäuser Verlag, Basel. 1966. x + 603 pp. 17.3 × 24.7 cm. 128 Swiss Francs.

We have come to look forward to each new volume in this series with pleasurable anticipation. These surveys contain some of the most adequate reviews of current interest in various medicinal fields, set against a historical background of developing ideas and experiments. It is disappointing to sense a foreboding about the future of medicinal chemistry in several leading articles in the present volume. The motivating basis of this attitude is, of course, the fact that medicinal discovery has slowed down; indeed, the last decade has been almost sterile compared to the surging tide of discovery from 1930 to 1955. Innovations since the mid-fifties have been largely developments and modifications based on earlier discoveries. Nobody will deny that few if any breakthroughs in drug research have appeared in the expanded medicinal literature of the last 10 years.

Some of the reasons for this decline have been extraneous and essentially at the clinical level: stricter regulation of drugs and their abuses, sparked by the tragedy of teratogenic side effects and by the smearing of the picture of drug studies and sales by politicians seeking reelection. But where there is smoke there is fire, and some of the abuses uncovered in the course of such discussions and the placebo nature of some widely advertised agents have contributed to the growing distrust of drugs by the public. But the real cause of the decimation of novel drug discovery has been the lack of acceptable and defendable new ideas which could be applied to the design of truly new drugs with a definite promise of carry-over from the laboratory to the clinic.

G. Ehrhart paints a particularly pessimistic picture of the present situation. He even discounts the value of molecular modification based on structure–activity relationships. His attitude may be limited by his emphasis on research achievements in his own company which, while noteworthy, do not represent the total scope of drug investigation. A much broader and more optimistic outlook is to be found in R. G. Denkewalter and Max Tishler's contemplations on the present and future of medicinal research. However, these authors also recognize the failure of current basic knowledge to spawn new ideas in therapeutic areas which have been resistant to advance so far. New insights must be gained from molecular biology, and the obvious conclusion is that we do not teach medicinal science of the future in our universities.

W. Kunz' review of new drugs is of value especially to the student of prescription items in Europe; the minimal additions to American drugs under the influence of restrictive legislation may have something to do with the local emphasis of this survey. J. H. Biel and B. K. B. Lum recount β-adrenergic blocking agents in Biel's usual masterful manner; the long and excellent article by E. J. Ariëns on the many facets of drug design complements the hopes expressed in the paper by the two Merck authors above. From the same company comes a particularly timely review of nonsteroid antiinflammatory agents by C. A. Winter. A critical evaluation of all the biological aspects of this important and therapeutically controversial field has long been needed.

The presentation of articles of general medicinal interest is an innovation to be welcomed in this series. These papers should persuade many medicinal chemists to place Volume 10 on their private book shelves.

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Topics in Medicinal Chemistry. Volume 1. Edited by J. L. RABINOWITZ and R. M. MYERSON. Interscience Division, John Wiley and Sons, Inc., New York, N. Y. 1967. xi + 453 pp. 24.5 × 17 cm. $17.75.

Edited monographs are usually compiled by coaxing contributors into writing chapters. Even though the original plan and outline prepared by the editors may represent a unified and timely effort, such plans are liable to fall by the wayside if key contributors drop out for some reason. If such an event endangers the publication of the book, some late substitution may be arranged in haste, and this will barely ever be as satisfactory as the original plan. Something like this must have happened to the present volume, or else a serious misunderstanding must have beset the choice and arrangement of the topics.

Medicinal chemistry and biochemical pharmacology have no quarrel how their fields of interest should be divided up. However, it is generally agreed that biologists gladly keep their fingers out of organic-preparative methodology, and medicinal chemists do the same when it comes to pharmacological methodology. There may be some occasional overlapping, but there is none when it comes to clinical pharmacology except for that rare species of a Ph.D. in chemistry who also holds an M.D. degree, and who actually works both as a chemist and as a clinician. I am sure that 99.9% of all medicinal chemists cannot aspire to such proficiency and would shy away from the legal and professional restrictions imposed on the physician who tests new drugs in patients. It is therefore strange to find a section on "Clinical Medicinal Chemistry" in the present book.

One of these chapters, on digitalis, lists the structural formulas, names, components, sources, etc., of the major cardiac glycosides which are of clinical importance, before delving into animal and human pharmacology of these substances. The formulas and names are merely descriptive; there is no attempt at correlation, at comparisons of structures and properties with activity, although these topics form the intellectual core of medicinal chemistry. It is worse in the chapter on oral contraceptives; it does not even have the formulas, and it is purely clinically oriented. This holds also for the descriptive chapter on radioactive drugs. The listing of the chemicals used in diagnostic procedures gives a

survey of the materials, to be sure, but that is not chemistry. The chapter on X-ray contrast agents is better in this regard.

The introductory chapter of the book on subcellular actions of cortisol in liver is pharmacology and biochemistry and looks strange under the heading, "Theoretical Concepts." Does that mean that biochemical remarks about the mode of action of drugs are theoretical in one chapter and applied in another?

Fortunately, the "Applied Medicinal Chemistry" section of the book *is* medicinal chemistry. It contains several good chapters (antiinflammatory agents by T. Y. Shen, chemical modification of antibiotics by S. J. Childress, antiviral agents by T. S. Osdene, antihypertensive agents by A. D. Bender, and thyroid and antithyroid drugs by H. A. Selenkow and M. S. Wool). The chapter on cancer chemotherapy by M. B. Shimkin is purely descriptive, clinically oriented, and of not much help for future researches.

It is to be hoped that the editors and publisher will be more critical in future volumes what they call medicinal chemistry. Half of the present book has abused and diluted the term, and such expansionist thrusts into nonchemical areas will not aid our thinking and our selection of reading material even in these days of interdisciplinary growth of science.

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Dilemmas in Drug Therapy. By HARRY BECKMAN. W. B. Saunders Co., Philadelphia, Pa. 1967. xi + 404 pp. 19 × 26.5 cm. $11.50.

A veteran American pharmacologist who serves as a consultant on drugs faces the following questions which almost any physician would ask an expert clinical pharmacologist: "Here is the patient and these are the circumstances. This drug has failed, and so has that. Who has used another unusual one and why? What are the risks? Is there something I should know and do not? What would you do?" The author offers experience, wisdom, and opinions in answers given by a physician, not by a computer. These answers cover 313 clinical subjects ranging over the whole area of medicine. Each subject is introduced by a detailed and straightforward question of several sentences. Then follows the author's answer, referenced where possible. Then comes another question and answer, and so forth. The opinions expressed are considerate, conservative, and carefully formulated and should be invaluable to the practicing physician in innumerable situations.

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Psychotropic Drugs and Related Compounds. By EARL USDIN and DANIEL H. EFRON. Sponsored by the Pharmacology Section, Psychopharmacology Research Branch, National Institute of Mental Health, Public Health Service, U. S. Department of Health, Education and Welfare. Public Health Service Publication No. 1589. U. S. Government Printing Office, Washington, D. C. 1967. iv + 367 pp. 24 × 16.7 cm. $2.75.

When a major field of medicinal research reaches a plateau and offers the investigator and clinician a bewildering array of similar agents for several areas and conditions, a referenced tabulation of virtually all drugs and agents (690 of them) comes as a most welcome gift to guide us at a glance through the burgeoning list of names, dosage forms, and applications. The term "gift" is appropriate; this book is offered at one-sixth or one-seventh the standard publisher's price for the number of pages and formulas, and although we recognize the taxpayer's contribution, the low price evokes nostalgic recollections of the days when individuals, and not just institutions, could afford a shelf full of professional books.

Both clinical drugs and all experimental compounds reported to have psychotropic activity were to be included; this ambitious goal had to be cut back arbitrarily, *e.g.*, all barbiturates were deleted. On the whole, however, almost all compounds with principally psychic activities can be found in this volume.

There exists no universally accepted system of nomenclature, and the authors have done a good job classifying compounds by popular naming schemes, by generic names, and by giving structural formulas. Virtually every synonym or trade name is listed, as well as names of manufacturers, distributors, and Registered Trade Mark users. Each entry contains LD_{50} values and human doses, where applicable, perhaps one of the most valuable features of this collection. Tranquilizing, antidepressant (energizing), and hallucinogenic activities are indicated, but no subclassification has been attempted. There are 985 literature references, 40 general references to media used in searching the literature of psychotropic drugs, an extensive compound index cross-referencing synonyms, an alphabetical list of manufacturers, and lists of abbreviations. Moreover, every owner of this book is promised a list of supplements until a new edition will be prepared. And all this for the price of a haircut.

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Problemès Actuels de Biochimie Appliqueé. Edited by M.-L. GIRARD. 1st series. Masson and Cie., Editeurs, Paris. 1967. vi + 368 pp. 16.5 × 24.5 cm. Paperback, 90 Francs.

This volume contains seven chapters concerned with some biochemical analytical processes, their background in physical chemistry, immunochemistry, pathology, biosynthetic pathways, and their application to diagnosis. In a discussion of gas exchanges on the pulmonary and cellular level, R. Bourdon touches upon phases of diabetes, anoxia, and other disorders traceable to contributory disturbances of acid–base equilibria. J. Canal takes up acid–base equilibria again in his chapter, the determination of the amount of NH_4^+ in biology, concentrating on ammonium ion metabolism and enzyme activity affected by it. A conservative chapter on serotonin and the biochemical exploration of its metabolism, well written, avoids speculation about the role of 5-HTA in organs where its significance is in question. However, the description of selective analytical methods for 5-HTA should aid in locating this compound and distinguishing it from accepted neurotransmitters. The remaining chapters also emphasize the analytical approach to biochemical researches. They are the exploration of electrophoretic results by the analyst and clinician (M.-L. Girard); errors in carbohydrate metabolism (F. Paolaggi); paraproteinemias: diagnosis, biochemistry, and immunochemistry (F. Rousselet); and dehydration states (J. Yonger and J. Saada) which so often cause infant mortality.

Any practicing biochemist who uses modern analytical techniques will find this book useful, especially if he can read elegant Parisian French with enjoyment.

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Design of Active-Site-Directed Irreversible Enzyme Inhibitors. By B. R. BAKER. John Wiley and Sons, Inc., New York, N. Y. 1967. xiii + 325 pp. 18 × 24.5 cm. $13.50.

Any scientist who publishes over 30 major articles per year in a field for whose growth he is principally responsible should assess his own work and that of others in the same area at given intervals. The book by "Bill" Baker, as he is known fondly among American medicinal chemists, fulfills this purpose in the field of irreversible enzyme inhibitors.

The first 15–20 years of metabolite antagonist studies centered around essentially reversible inhibitors, but scored successes only in a few selected cases. The reason for this over-all failure was lack of selectivity. In an irreversible inhibitor attached to the active site of an enzyme plus some other location at the enzyme surface, an extra dimension of specificity has been introduced which can distinguish between even closely related isoenzymes. Since the three-dimensional conformation of enzymes is still mostly unknown, we cannot design an antagonist *a priori* to fit a site surrounded by those spatially neighboring groups to which the enzyme owes its rapid rate of reaction. Therefore, patient mapping of such amorphously visualized humps or cavities is necessary by systematic alteration of the structure of the inhibitor and by carrying out thousands of kinetic measurements of residual enzyme activity. From these data at least some conclusions have been drawn concerning the structure of selective inhibitors and the role and location of polar, bulky, and hydrophobic groups in their molecules. It is a tedious way of mapping